Year: 2018

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DOI: https://doi.org/10.1097/WNR.0000000000001012

Originally published at:
Thomas, Felix A; Dietz, Volker; Scharfenberger, Thiemo; Schrafl-Altermatt, Miriam (2018). Cooperative hand movements: effect of a reduced afference on the neural coupling mechanism. NeuroReport, 29(8):650-654.
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Cooperative hand movements: effect of a reduced afference on the neural coupling mechanism

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The aim of this study was to evaluate the influence of unilateral reduction of afferent input on the 'neural coupling' mechanism during cooperative hand movements. This 'neural coupling' is reflected in the task-specific appearance of contralateral reflex responses in forearm muscles to unilateral arm nerve stimulation. Sensory input from the right hand was reduced by ischemic nerve block at the right wrist. Ipsilateral and contralateral reflex responses elicited by stimulation of the ulnar nerve either at the left or the right wrist proximal to the nerve block were recorded in forearm extensors during the performance of cooperative hand movements. During ischemia of the right hand, a significant difference was found in the magnitude of the contralateral responses, that is, contralateral reflex responses in the right arm were significantly higher compared with the left arm (*P* = 0.04). Ipsilateral reflex responses were not affected by ischemic nerve block. The reduced afference from the ischemic hand during cooperative hand movements is assumed to weaken the activity in ipsilateral pathways involved in the neural coupling mechanism. Consequently, a shift in the interhemispheric balance might lead to the relative increase and decrease in the contralateral responses to left and right nerve stimulation, respectively. The study provides novel information on the involvement of ipsilateral hemispheres in the performance of cooperative hand movements. ***NeuroReport*** **00:000–000**

NeuroReport 2018, **00**:000–000

Keywords: contralateral reflex responses, cooperative hand movements, ischemic nerve block, neural coupling

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Received 7 February 2018 **accepted** 23 February 2018

Introduction

Most studies on upper limb motor control have focused on unimanual or bimanual noncooperative (e.g. prosupination) hand movements [1,2]. However, a number of activities of daily living, such as opening a bottle, require cooperative hand movements. It has been discovered that cooperative hand movements underlie a task-specific neural coupling mechanism that is not involved in the control of other bimanual movement tasks [3]. This task-specific coupling is reflected in the occurrence of bilateral electromyographic (EMG) reflex responses following unilateral arm nerve stimulation [3,4]. Furthermore, an functional MRI study reported extra-activation and functional coupling of bilateral secondary somatosensory (S2) cortical areas [3]. It appears that the shared sensory input from each hand to both hemispheres [5] is integrated and processed in S2 areas, which plays a key role in the task-specific neural coupling. In addition, increased amplitudes of ipsilateral somatosensory evoked potentials [6,7] indicate an involvement of ipsilateral and contralateral hemispheres in the neural coupling of cooperative hand movements.

The objective of this study was to explore the effect of an artificially reduced afference because of ischemic nerve block (INB) from the right hand during cooperative hand movements on contralateral reflex responses and thus on the neural coupling mechanism.

INB is a technique to induce a transient reduction in sensory perception and, consequently, in ascending drive to the brain [8–13].

It is hypothesized that the amplitudes of contralateral reflex responses following unilateral nerve stimulation are reduced in both right and left forearm muscles. This hypothesis is based on the assumption that ipsilateral and contralateral afferent pathways are involved in the neural coupling mechanism [3,6] and that disruption of the balance between the two hemispheres can lead to changes in the neural coupling [4]. Accordingly, partial blocking of group I afferents of one hand was expected to lead to a bilateral reduction of reflex responses to unilateral nerve stimulation.

Participants and methods

This study was approved by the local Ethics Committee of the Canton of Zürich and conformed to the standards set by the declaration of Helsinki. Before the experiment, all participants provided written informed consent. Twenty-four healthy individuals (15 women) with a mean age of 26 ± 3.1 years were included.

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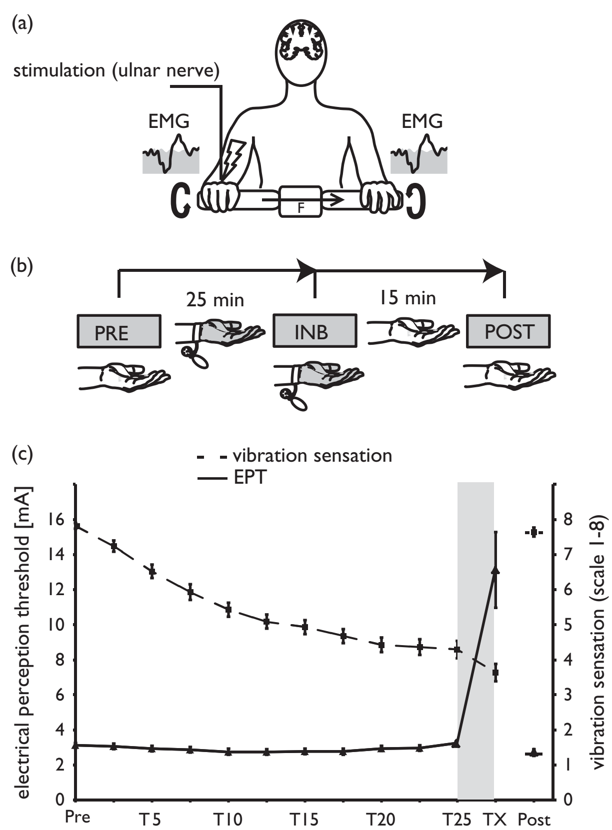
Experimental protocol

The protocol comprised the recording of EMG reflex responses in the ipsilateral and contralateral forearm extensor muscles to unilateral ulnar nerve stimulation during cooperative hand movements before (PRE), during (INB), and after (POST) ischemia of the right hand (Fig. 1a and b). In all conditions, volunteers were lying in a supine position. Cooperative hand movements (mimicking bottle opening and closing movements) were achieved by alternating rhythmic counteractive wrist flexion and extension movements (one movement cycle 1.33 s) on a device similar to that described previously [3, 4]. The order of side of nerve stimulation was pseudorandomized, that is, stimulations were applied first either at the right or left ulnar nerve during PRE, INB, and POST conditions, but the order was consistent throughout the conditions. Thus, the experiment consisted of six recording blocks (i.e. one block for each condition and side of stimulation). Throughout the experiment, the changes in the individual sensory perception were monitored.

Fig. 1



(a) Experimental setup. Stimulations were applied during cooperative hand movements. The handles of the device are mechanically coupled, that is, during cooperative hand movements, the torque produced from one limb has to be counteracted by the other limb. (b) Experimental protocol. Movement conditions were performed before (PRE), during (INB), and after (POST) ischemic nerve block (INB). (c) Course of sensory perception during INB. Left axis: Electrical perception threshold (EPT). Right axis: Vibration sensation. The gray bar shows the time period of the 'INB' condition where reflex responses were recorded. This period (about 10 min) lasted until TX (i.e. release of INB). Error bars represent the SE. Note that for EPT PRE–T25 triangles overlap the error bars. EMG, electromyography.

Electrical nerve stimulation

Participants were stimulated 15 times every 3–8 s in each of the experimental conditions. The stimuli were used to evoke EMG reflex responses in the right and left extensor carpi radialis muscle. Stimulations were triggered randomly within the movement cycles. They were applied by a KeyPoint Focus (Natus, Pleasanton, California, USA) through self-adhesive surface electrodes (Ambu A/S Neuroline 700; Ambu A/S, Ballerup, Denmark) that were placed over the ulnar nerve at the wrist on the left side and proximal to ischemia on the right side with an interelectrode distance of 2 cm (cathode proximal to anode). Stimulation intensity was set to 150% of the motor threshold (MT), that is, the lowest intensity resulting in a visible twitch of the abductor digiti minimi muscle. Stimulations consisted of a burst of four biphasic pulses of 1 ms duration per pulse, each separated by 2 ms, resulting in a total stimulus duration of 10 ms.

Electromyographic recordings

EMG activity of the extensor carpi radialis of both forearms was recorded (proximal to ischemia) using disposable self-adhesive AG/AgCl dual surface electrodes with an interelectrode distance of 1.75 cm (Noraxon, Scottsdale, Arizona, USA). Data were sampled (1500 Hz), band-pass filtered (10–10 000 Hz), and postprocessed as described previously [4]. The root mean square (RMS) of the rectified EMG signal was calculated for the time window between 75 and 135 ms after stimulus onset as this period is known to include the main components of the late (i.e. N2, P2) ipsilateral and contralateral reflex response [3]. The RMS values were normalized by dividing them by the RMS of the rectified background activity calculated over the prestimulus time window from -30 to -10 ms.

Ischemic nerve block

INB was achieved by a pneumatic tourniquet applied at the right wrist. The tourniquet was inflated after the PRE condition above systolic pressure (250 mmHg) and was maintained constant until completion of the reflex recordings of the INB condition, which was started after 25 min of ischemia and lasted over about 10 min. Subsequently, the tourniquet was released and participants recovered for 15 min before the POST condition was performed.

Sensory perception monitoring

During the 25 min of INB, sensory perception of the right hand declined. During this phase and during the

15-min recovery phase after INB, sensory perception was assessed every 2.5 min (Fig. 1c). Two different methods were used to assess perception: electrical perception threshold (EPT) and vibration sensation (VS). For EPT, electrical stimulations were applied at the palmar side of the right middle finger with a frequency of 3.1 Hz with stepwise increasing intensity until the participant reported a sensation (average of three trials). For VS, a tuning fork was applied at the metacarpophalangeal joint of the right middle finger until the participant reported the cessation of VS (scale ranging from 8 to 1, where 8 is normal perception).

Statistical analysis

Data processing and analysis were carried out using MatLab v. 2013b (Mathworks, Natick, Massachusetts, USA) and Soleasy (Alea Solutions GmbH, Zurich, Switzerland). SPSS, version 23 (IBM Statistics, Chicago, Illinois, USA) was used for all statistical procedures. After log10 transformation, differences in the normalized RMS of the EMG reflex responses for the entire sample were calculated using a 2×3 repeated-measures analysis of variance (ANOVA) [stimulation side (right, left)$\times$ conditions (PRE, INB, POST)] with interaction. Side differences in MT and post-hoc tests were performed using paired t-tests corrected for multiple comparisons with Bonferroni's correction. Corrected P values below 0.05 were considered significant. In addition, effect sizes were calculated for the ANOVA as partial eta-squared ($\eta_P{}^2$) and for paired t-tests as Cohen's d. If not stated otherwise, all values are given as mean $\pm$ SD.

Results

Three participants had to be excluded from further evaluation: one because of discomfort during ischemia, one because of problems in executing the movements properly, and one because of technical problems. Therefore, data from 21 participants were analyzed. All volunteers perceived the electrical stimulations at 150% MT as non-noxious. The MT assessed at the beginning of the experiment differed significantly between the sides (MT left: 3.6 ± 0.2 mA; MT right: 4.2 ± 1.0 mA, $P=0.007$, $d=0.613$). This difference can be explained by the placement of the stimulation electrode proximal of the tourniquet on the right side. Nevertheless, the normalized reflex responses (i.e. ipsilateral and contralateral) during the PRE condition did not differ between the sides. On average, the ischemia was maintained over 36.5 ± 1.8 min. The time point of release of INB is referred to as TX (Fig. 1c).

Reduced sensory perception

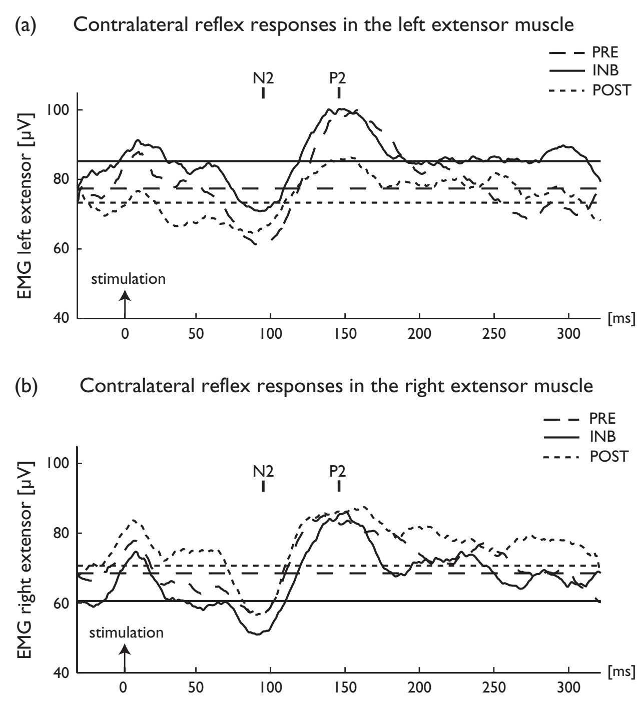
EPTs started at 3.0 ± 0.7 mA before the PRE condition and amounted to 3.24 ± 0.7 mA before INB. A steep increase in EPT occurred from T25 to TX, that is, during the INB condition, resulting in an EPT of 13.3 ± 10.1 mA after the INB condition. VS was 7.8 ± 0.36 at the beginning of the experimental procedure and decreased almost linearly during ischemia, resulting in a VS of 4.2 ± 1.1 before and 3.6 ± 1.1 after the INB condition, respectively. After TX, when INB was released, both EPT and VS returned to baseline values.

Ipsilateral and contralateral muscle reflex responses

Figure 2a shows the grand averages ($n=21$) of the contralateral EMG reflex responses in the left forearm extensor muscle during the three experimental conditions (PRE, INB, and POST) of cooperative hand movements. All responses were clearly above the respective level of background EMG. During INB, contralateral reflex responses in the left arm were smaller compared with PRE. In contrast, the contralateral reflex response in the right extensor was increased during INB compared with PRE (Fig. 2b). These differences were not statistically significant.

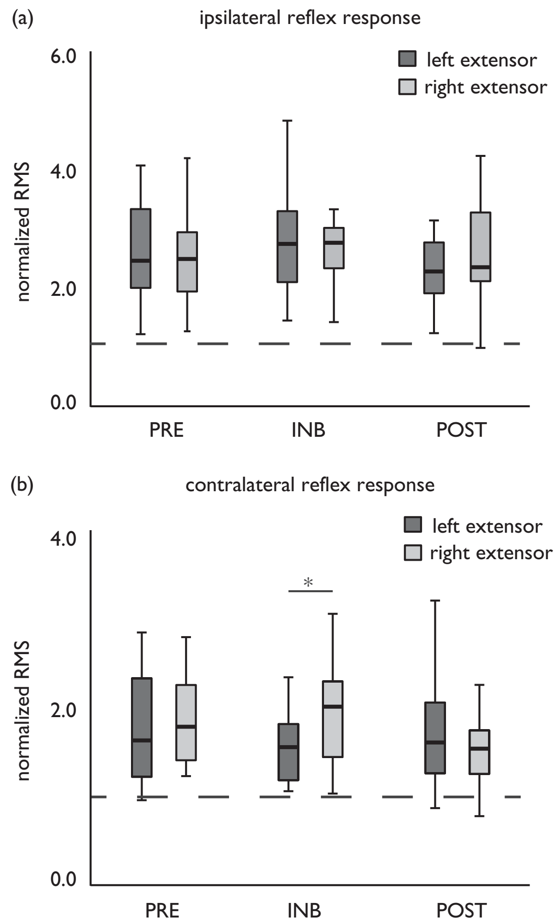
In Fig. 3, the quantitative data of the extensor reflex responses (expressed as reflex RMS normalized to the background activity RMS) are shown. No significant effect of INB could be observed in ipsilateral reflex responses, either in the right (PRE: 2.45 ± 0.74; INB:

Fig. 2



Grand averages ($n=21$) of contralateral reflex responses recorded before (PRE), during (INB), and after (POST) ischemic nerve block (INB). (a) Contralateral reflex responses in the left forearm extensor muscle (i.e. stimulation of the right ulnar nerve). (b) Contralateral reflex responses in the right forearm extensor muscle (i.e. stimulation of the left ulnar nerve). Horizontal lines show the respective root mean square value of the background activity. N2 and P2 mark the peaks of the reflex responses. EMG, electromyography.

Fig. 3



Quantitative root mean square (RMS) values of ipsilateral and contralateral reflex responses normalized to the background activity before (PRE), during (INB), and after (POST) ischemic nerve block (INB). The quantified averages of the reflex electromyographic responses in the forearm extensor muscle from the entire participant sample ($n = 21$) are shown (a) ipsilateral and (b) contralateral to the site of stimulation. The dashed horizontal line shows the background activity. Boxes represent the interquartile range (25th–75th percentile) separated by the median. $^*P < 0.05$, indicate a significant difference.

2.74 ± 0.99; POST: 2.76 ± 1.41) or in the left (PRE: 2.62 ± 1.03; INB: 3.45 ± 3.35; POST: 2.38 ± 0.83) extensor [side: $F(1,20) = 0.26$, $P = 0.80$, $\eta_P^2 = 0.003$; conditions: $F(2,40) = 1.59$, $P = 0.23$, $\eta_P^2 = 0.14$; side × condition: $F(2,40) = 1.15$, $P = 0.33$, $\eta_P^2 = 0.11$]. For contralateral reflex responses, repeated-measures ANOVA showed a significant interaction effect of side and condition [$F(2,40) = 3.99$, $P = 0.02$, $\eta_P^2 = 0.17$]. Post-hoc tests indicate that this interaction effect is because of the significant difference in the right (PRE: 1.95 ± 0.66; INB: 2.22 ± 1.1; POST: 1.54 ± 0.42) and left (PRE: 2.02 ± 1.46; INB: 1.57 ± 0.40; POST: 1.86 ± 1.04) extensor muscles during INB ($P = 0.04$, $d = 0.265$). Here, we observe increased reflex responses in the right extensors compared with reduced responses in the left extensors (Fig. 3b). However, ANOVA showed no significant main effects for either the side of stimulation [$F(1,20) = 0.99$, $P = 0.33$, $\eta_P^2 = 0.05$] or the condition [$F(2,40) = 2.36$, $P = 0.108$, $\eta_P^2 = 0.11$].

Discussion

The aim of this study was to explore the influence of reduced afferent input from the right hand, achieved by INB, on the neural coupling mechanism underlying cooperative hand movements. The main result consisted of significantly increased contralateral reflex responses in the right compared with the left arm during INB. Ipsilateral reflex responses were neither different between the sides nor the PRE, INB, and POST conditions.

INB on an upper limb is known to induce short-term changes in the sensorimotor cortex including an increased output to muscles proximal to ischemia following transcranial magnetic stimulation during rest [8, 14,15]. Translated to our study, enhanced reflex responses in right forearm extensors would be expected to occur. This was, however, only true for contralateral responses and not for ipsilateral ones. The lack of general increase in muscle responses proximal to INB in our study was most probably because of the dynamic movement conditions used here. It has been shown that increased muscle responses can only be observed in resting muscles, an effect that becomes lost with muscle activation [15,16]. Therefore, the increase in contralateral reflex responses cannot be explained by known INB effects, that is, the modulation of reflex amplitude found here seems to be specific for the neural coupling.

In view of our hypothesis, the side difference in reflex amplitude modulation was unexpected. We only partially succeeded with our goal to further elucidate the pathways involved in neural coupling. The main finding might best be interpreted on the basis of the observations made so far, that is, the essential role of ipsilateral hemispheres in the neural coupling mechanism. The enlarged ipsilateral somatosensory evoked potential during cooperative hand movements [6] indicates an enhanced afferent inflow to the ipsilateral hemisphere that becomes task-specifically processed in the S2 cortical areas [3]. This area is known to exchange and integrate the afferent input from both hands [3,17], leading to interhemispheric unification [18]. In this study, the afferent input from the right hand is reduced compared with that from the left hand. It is assumed that this asymmetrical afferent input from the hands causes a bias in the unification. Thus, during INB, an imbalance in the functional coupling of S2 areas is expected to occur [3], leading also to an imbalance in the generation of the contralateral reflex responses. The reduced contralateral response in the left forearm extensors might be caused by an attenuation of neural coupling from the right to the left side because of the reduced afference originating from the right cooperating hand. As a consequence, the increase in the contralateral reflex amplitude in the right forearm extensors might be because of a shift in the interhemispheric balance [8,19].

An interesting aspect of this study is that the effects of INB were only related to the behavior of contralateral reflex responses. This confirms previous findings of task-specific activation of ipsilateral pathways during cooperative hand movements by an interaction of the two hemispheres. A shift in balance between the hemispheres might impact the bilateral efferent reflex output.

Despite the sensory deficit of one hand, distinct contralateral reflex responses occurred irrespective of the site of stimulation, that is, the neural coupling remained preserved. In contrast, neural coupling was strongly impaired, with absent contralateral reflex responses in stroke patients when the affected arm with slight sensory deficit was stimulated [4]. This difference might be because of an impaired processing of sensory information in the affected hemisphere [20].

Conclusion

This study underlines the significance of the interaction between ipsilateral and contralateral hemispheres in the control of cooperative hand movements by a neural coupling mechanism. The study shows that a reduced sensation of one hand during cooperative movements leads to an imbalance in the processing and interhemispheric unification of the shared bimanual afferent input. Consequently, the distribution of bilateral reflex output to unilateral nerve stimulation is asymmetrical.

Acknowledgements

F.A.T. carried out the data acquisition analysis and helped in drafting the manuscript; T.S. helped with data acquisition and interpretation of the results; V.D. and M.S. designed the study, interpreted the results, and participated in writing the manuscript. All authors read and approved the final manuscript.

This work was supported by the Swiss National Foundation (PMPDP3_164464/1) and the European Institute of Innovation & Technology – Health (17518).

Conflicts of interest

There are no conflicts of interest.

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